

What is claimed:

1. A compound comprising the structure:



5 wherein each Y represents a tyrosine; each D represents an aspartic acid, each I represents an isoleucine; and each N represents an asparagine; wherein  $\alpha$  represents from 0 to 9 amino acids, with the proviso that if there are more than 2 amino acids, they are joined by peptide bonds in consecutive order and have a sequence identical to the sequence set forth in SEQ ID NO: 1 beginning with the I at position 9 and extending therefrom in the amino terminal direction; 10 wherein  $\beta$  represents from 0 to 14 amino acids, with the proviso that if there are more than 2 amino acids, they are joined by peptide bonds in consecutive order and have a sequence identical to the sequence set forth in SEQ ID NO: 1 beginning with the E at position 18 and extending therefrom in the carboxy terminal direction; 15 wherein  $\theta$  represents an amino group or an acetylated amino group; wherein  $\lambda$  represents a carboxyl group or an amidated carboxyl group; wherein all of  $\alpha, Y, D, I, N, Y, Y, T, S$  and  $\beta$  are joined together by peptide bonds; 20 25 further provided that at least two tyrosines in the compound are sulfated.

2. The compound of claim 1, wherein  $\beta$  represents less

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12. The compound of claim 1, wherein  $\beta$  represents less than 7 amino acids.
13. The compound of claim 1, wherein  $\beta$  represents less than 6 amino acids.
14. The compound of claim 1, wherein  $\beta$  represents less than 5 amino acids.
15. The compound of claim 1, wherein  $\beta$  represents less than 4 amino acids.
16. The compound of claim 1, wherein  $\beta$  represents less than 3 amino acids.
17. The compound of claim 1, wherein  $\beta$  represents less than 2 amino acids.
18. The compound of claim 1, wherein  $\beta$  represents less than 1 amino acid.
19. The compound of claim 1, wherein  $\alpha$  represents less than 9 amino acids.
20. The compound of claim 1, wherein  $\alpha$  represents less than 8 amino acids.
21. The compound of claim 1, wherein  $\alpha$  represents less than 7 amino acids.

22. The compound of claim 1, wherein  $\alpha$  represents less than 6 amino acids.
- 5 23. The compound of claim 1, wherein  $\alpha$  represents less than 5 amino acids.
24. The compound of claim 1, wherein  $\alpha$  represents less than 4 amino acids.
- 10 25. The compound of claim 1, wherein  $\alpha$  represents less than 3 amino acids.
26. The compound of claim 1, wherein  $\alpha$  represents less than 2 amino acids.
- 15 27. The compound of claim 1, wherein  $\alpha$  represents less than 1 amino acid.
28. A composition comprising the compound of claim 1 and a detectable marker attached thereto.
- 20 29. The composition of claim 28, wherein the detectable marker is biotin.
- 25 30. The composition of claim 28, wherein the detectable marker is attached at the C-terminus of the compound.
31. A composition which comprises a carrier and an

amount of the compound of claim 1 effective to inhibit binding of HIV-1 to a CCR5 receptor on the surface of a CD4+ cell.

- 5      32. A method of inhibiting human immunodeficiency virus infection of a CD4+ cell which also carries a CCR5 receptor on its surface which comprises contacting the CD4+ cell with an amount of the compound of claim 1 effective to inhibit binding of human immunodeficiency virus to the CCR5 receptor so as to thereby inhibit human immunodeficiency virus infection of the CD4+ cell.
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- 15      33. The method of claim 32, wherein the CD4+ cell is present in a subject and the contacting is effected by administering the compound to the subject.
- 20      34. A method of preventing CD4+ cells of a subject from becoming infected with human immunodeficiency virus which comprises administering to the subject an amount of the compound of claim 1 effective to inhibit binding of human immunodeficiency virus to CCR5 receptors on the surface of the CD4+ cells so as to thereby prevent the subject's CD4+ cells from becoming infected with human immunodeficiency virus.
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35. A method of treating a subject whose CD4+ cells are infected with human immunodeficiency virus which

comprises administering to the subject an amount of the compound of claim 1 effective to inhibit binding of human immunodeficiency virus to CCR5 receptors on the surface of the subject's CD4+ cells so as to thereby treat the subject.

36. The method of any one of claims 33-35, wherein the compound is administered by aerosol, intravenous, oral or topical route.

37. The method of claim 33 or 35, wherein the subject is infected with HIV-1 prior to administering the compound to the subject.

38. The method of claim 33 or 34, wherein the subject is not infected with HIV-1 prior to administering the compound to the subject.

39. The method of claim 38, wherein the subject is not infected with, but has been exposed to, human immunodeficiency virus.

40. The method of any one of claims 33-35, wherein the effective amount of the compound comprises from about 1.0 ng/kg to about 100 mg/kg body weight of the subject.

41. The method of claim 40, wherein the effective amount of the compound comprises from about 100

ng/kg to about 50 mg/kg body weight of the subject.

42. The method of claim 41, wherein the effective  
amount of the compound comprises from about 1  $\mu$ g/kg  
to about 10 mg/kg body weight of the subject.

43. The method of claim 42, wherein the effective  
amount of the compound comprises from about 100  
 $\mu$ g/kg to about 1 mg/kg body weight of the subject.

44. The method of any one of claims 33-35, wherein the  
subject is a human being.

45. A method of identifying an agent which inhibits  
binding of a CCR5 ligand to a CCR5 receptor which  
comprises:

- (a) immobilizing the compound of claim 1 on a  
solid support;
- (b) contacting the immobilized compound from step  
(a) with sufficient detectable CCR5 ligand to  
saturate all binding sites for the CCR5 ligand  
on the immobilized compound under conditions  
permitting binding of the CCR5 ligand to the  
immobilized compound so as to form a complex;
- (c) removing any unbound CCR5 ligand;
- (d) contacting the complex from step (b) with the  
agent; and
- (e) detecting whether any CCR5 ligand is displaced  
from the complex, wherein displacement of

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(f) comparing the amount of CCR5 ligand bound to the compound in step (e) with the amount measured in step (c), wherein a reduced amount measured in step (e) indicates that the agent binds to the compound so as to thereby



identify the agent as one which inhibits binding of the CCR5 ligand to the CCR5 receptor.

5      47. A method of identifying an agent which inhibits binding of a CCR5 ligand to a CCR5 receptor which comprises:

- 10      (a) immobilizing the compound of claim 1 on on a solid support;
- 15      (b) contacting the immobilized compound from step (a) with the agent and detectable CCR5 ligand under conditions permitting binding of the CCR5 ligand to the immobilized compound so as to form a complex;
- 20      (c) removing any unbound CCR5 ligand;
- 25      (d) measuring the amount of detectable CCR5 ligand which is bound to the immobilized compound in the complex;
- (e) measuring the amount of detectable CCR5 ligand which binds to the immobilized compound in the absence of the agent;
- (f) comparing the amount of CCR5 ligand which is bound to the immobilized compound in step (e) with the amount measured in step (d), wherein a reduced amount measured in step (d) indicates that the agent binds to the compound or CCR5 ligand so as to thereby identify the agent as one which inhibits binding of the CCR5 ligand to the CCR5 receptor.

48. The method of claim 47, wherein the amount of the detectable ligand in step (a) and step (e) is sufficient to saturate all binding sites for the CCR5 ligand on the compound.

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49. A method of identifying an agent which inhibits binding of a CCR5 ligand to a CCR5 receptor which comprises:

- 10 (a) contacting the compound of claim 1 with the agent and detectable CCR5 ligand under conditions permitting binding of the CCR5 ligand to the compound so as to form a complex;
- 15 (b) removing any unbound CCR5 ligand;
- (c) measuring the amount of detectable CCR5 ligand which is bound to the compound in the complex;
- (d) measuring the amount of detectable CCR5 ligand which binds to the compound in the absence of the agent;
- 20 (e) comparing the amount of CCR5 ligand which is bound to the compound in step (c) with the amount measured in step (d), wherein a reduced amount measured in step (c) indicates that the agent binds to the compound or CCR5 ligand so
- 25 as to thereby identify the agent as one which inhibits binding of the CCR5 ligand to the CCR5 receptor.

50. The method of claim 49, wherein the amount of the

detectable ligand in step (a) and step (d) is sufficient to saturate all binding sites for the CCR5 ligand on the compound.

- 5 51. The method of any one of claims 45-50, wherein the detectable CCR5 ligand is labeled with a detectable marker.
- 10 52. A method of identifying an agent which inhibits binding of a CCR5 ligand to a CCR5 receptor which comprises:
- 15 a) immobilizing the compound of claim 1 on a solid support;
- b) contacting the immobilized compound from step a) with the agent dissolved or suspended in a known vehicle and measuring the binding signal generated by such contact;
- 20 c) contacting the immobilized compound from step a) with the known vehicle in the absence of the compound and measuring the binding signal generated by such contact;
- 25 d) comparing the binding signal measured in step b) with the binding signal measured in step c), wherein an increased amount measured in step b) indicates that the agent binds to the compound so as to thereby identify the agent as one which binds to the CCR5 receptor.

53. The method of claim 52, wherein the solid support

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is a surface plasmon resonance sensor chip.

54. The method of claim 52 or 53, wherein the binding signal is measured by surface plasmon resonance.

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55. A method of obtaining a composition which comprises:

10 (a) identifying a compound which inhibits binding of a CCR5 ligand to a CCR5 receptor according to the method of any one of claims 45-50 and 52; and

(b) admixing the compound so identified or a homolog or derivative thereof with a carrier.

15 56. The method of any one of claims 45-50 and 52, wherein the CCR5 ligand is a complex comprising an HIV-1 envelope glycoprotein and a CD4-based protein.

20 57. The method of claim 56, wherein the HIV-1 envelope glycoprotein is gp120, gp140 or gp160.

58. The method of claim 56, wherein the CD4-based protein is soluble CD4 or CD4-IgG2.

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59. The method of any one of claims 45-50 and 52, wherein the CCR5 ligand is a chemokine.

60. The method of claim 59, wherein the chemokine is

RANTES, MIP-1 $\alpha$  or MIP-1 $\beta$ .

61. The method of any one of claims 45-50 and 52, wherein the CCR5 ligand is an antibody.

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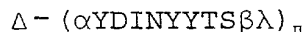
62. The method of claim 61, wherein the antibody is selected from the group consisting of PA8 (ATCC Accession No. HB-12605), PA10 (ATCC Accession No.12607), PA11 (ATCC Accession No. HB-12608), PA12 (ATCC Accession No. HB-12609).

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63. The method of claim 45 or 47, wherein the solid support is a microtiter plate well, a bead or surface plasmon resonance sensor chip.

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64. A compound having the structure:



wherein each T represents a threonine, each S represents a serine, each Y represents a tyrosine; each D represents an aspartic acid, each I represents an isoleucine; and each N represents an asparagine;

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wherein  $\alpha$  represents from 0 to 9 amino acids, with the proviso that if there are more than 2 amino acids, they are joined together by peptide bonds in consecutive order and have a sequence identical to the sequence set forth in SEQ ID NO: 1 beginning with the I at position 9 and extending therefrom in the amino terminal direction;

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wherein  $\beta$  represents from 0 to 14 amino acids, with the proviso that if there are more than 2 amino acids, they are joined together by peptide bonds in consecutive order and have a sequence identical to the sequence set forth in SEQ ID NO: 1 beginning with the E at position 18 and extending therefrom in the carboxy terminal direction;

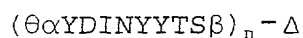
wherein  $\lambda$  represents a carboxyl group or an amidated carboxyl group;

wherein all of  $\alpha, Y, D, I, N, Y, Y, T, S$  and  $\beta$  are joined together by peptide bonds,

further provided that at least two tyrosines in the compound are sulfated,

wherein  $n$  is an integer from 1 to 8,  $\Delta$  is a polymer, and the solid line represents up to 8 linkers which attach the structure in parentheses to  $\Delta$ .

65. A compound having the structure:



wherein each T represents a threonine, each S represents a serine, each Y represents a tyrosine; each D represents an aspartic acid, each I represents an isoleucine; and each N represents an asparagine;

wherein  $\alpha$  represents from 0 to 9 amino acids, with the proviso that if there are more than 2 amino acids, they are joined together by peptide bonds in consecutive order and have a sequence identical to

the sequence set forth in SEQ ID NO: 1 beginning with the I at position 9 and extending therefrom in the amino terminal direction;

wherein  $\beta$  represents from 0 to 14 amino acids, with the proviso that if there are more than 2 amino acids, they are joined together by peptide bonds in consecutive order and have a sequence identical to the sequence set forth in SEQ ID NO: 1 beginning with the E at position 18 and extending therefrom in the carboxy terminal direction;

wherein  $\theta$  represents an amino group or an acetylated amino group;

wherein all of  $\alpha, Y, D, I, N, Y, Y, T, S$  and  $\beta$  are joined together by peptide bonds,

further provided that at least two tyrosines in the compound are sulfated,

wherein  $n$  is an integer from 1 to 8,  $\Delta$  is a polymer, and the solid line represents up to 8 linkers which attach the structure in parentheses to  $\Delta$ .

66. The compound of claim 64 or 65, wherein the polymer is selected from the group consisting of a linear lysine polymer, a branched lysine polymer, a linear arginine polymer, a branched arginine polymer, polyethylene glycol, a linear acetylated lysine polymer, a branched acetylated lysine polymer, a linear chloroacetylated lysine polymer and a branched chloroacetylated lysine polymer.